

U.S. Serial No. 09/747,774

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REMARKS

Claims 1, 2, 5, 8-11, 17, 25-27, 36, 37, 39, 50, 51, 53, 77 and 78 are pending in the application. No amendments to the claims are presented herein.

Declaration under 37 C.F.R. § 1.132

Applicants file concurrently herewith the Declaration of Mark Poznansky, M.D., Ph.D. pursuant to 37 C.F.R. § 1.132 for the Examiner's consideration.

Rejection of Claims Under 35 U.S.C. § 101

Claims 1, 2, 5, 8-11, 17, 25-27, 36, 37, 39, 50, 51, 53, 77 and 78 are rejected under 35 U.S.C. § 101 as not supported by either a specific and substantial asserted utility or a well established utility. Applicants respectfully traverse the rejection for the reasons of record set forth in the responses filed on January 2, 2004, October 19, 2004 and April 11, 2005 and for the further reasons discussed in detail below.

Claims 1, 2, 5, 8-11, 17, 25-27, 36, 37, 39, 50, 51, 53, 77 and 78 are directed to recombinant yeast cells comprising a recombinant gene encoding a heterologous orphan G protein-coupled receptor wherein the receptor is expressed on the cell membrane of the cell such that signal transduction activity is modulated by interaction with an extracellular signal; and a recombinant gene encoding a heterologous test polypeptide, wherein the test polypeptide is transported to a location allowing interaction with the receptor expressed on the cell membrane. The yeast cells are "autocrine" in that they are engineered to express the polypeptides to be tested for the ability to modulate the orphan G protein-coupled receptors expressed by the yeast cells. A mixture of such yeast cells can be used to express a library of test polypeptides. The claimed recombinant yeast cells are used in screening assays to identify compounds, e.g., ligands that modulate the orphan G protein-coupled receptors expressed by the yeast cells.

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The Examiner has rejected the claims as not supported by either a specific and substantial asserted utility or a well-established utility, citing the reasons of record. The Examiner additionally objects to the Applicant's response of April 11, 2005 on the grounds that the "instant invention lacks specific and substantial real world utility absent elucidation of the biological function of the orphan receptor and any role that the ligands identified as modulators of the receptor would play in modulation or identification of any disease state associated with that biological function." (Office Action dated June 14, 2005, page 3, first paragraph.)

The Applicants respectfully traverse the rejection.

A. *Orphan G Protein-Coupled Receptors Have a Well-known Biological Function*

G protein-coupled receptors, including the orphan G protein-coupled receptors of the present invention, have a well-known biological function in cells, as described in the accompanying Declaration of Mark Poznansky, M.D., Ph.D. (the "Declaration") and the previous response filed on April 11, 2005. G protein-coupled receptors enable ligands to trigger G protein activation, which in turn modulates the activity of an effector (e.g., adenylyl cyclase). This activity is a common biological function among all G protein-coupled receptors, including orphan G protein-coupled receptors, that was known in the art at the time that the present application was filed. Thus, identifying ligands that signal or inhibit signaling through orphan G proteins is both specific and substantially useful where modulation of this kind of intracellular biological response is desired.

Applicants' previous response, filed on April 11, 2005 addressed this point in great detail (Office Action Response dated April 11, 2005, page 8, second full paragraph through page 9). However, the instant Office Action fails to address this point and is, therefore, non-responsive. No reasoning whatsoever has been provided for failing to acknowledge the biological function of orphan G protein-coupled receptors, particularly in the modulation of adenylyl cyclase. A complete response is not only requested, but also required. *See M.P.E.P. § 2142. Because the instant Office Action is non-*

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responsive for failure to address this very important point, Applicants respectfully request that the Examiner withdraw the finality of the instant Office Action.

Applicants submit the Declaration as evidence that those of ordinary skill in the art recognize the utility of the claimed invention based on the known benefit of identifying ligands of orphan G protein-coupled receptors. The Declaration represents an opinion from a qualified expert who conducts research relating to G protein-coupled receptor signaling and who concludes, based upon relevant facts, that the claimed invention is associated with a well-known and specific biological function and is useful within the meaning of § 101 for the identification of ligands that modulate that function. In the Declaration, Dr. Poznansky clearly states:

"[T]he specific biological function of orphan G-protein coupled receptors is well established inasmuch as the biological function of G protein-coupled receptors, including orphan G-protein coupled receptors, enables ligands to modulate the intracellular activity of adenylyl cyclase and phospholipase C. Therefore, the orphan G-protein receptors described in the present application have a common, specific and well-known biological function in cells."
(Declaration, p. 4, para. 9.)

Applicants submit that the Declaration must be given substantial consideration. The following section of the M.P.E.P. provides further guidance on the subject:

2107 Guidelines for Examination of Applications

An invention has a well established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible.... *If the applicant has asserted that the claimed invention is useful for any particular practical purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."*

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A rejection based on lack of utility should not be maintained if an asserted utility for the claimed invention would be considered specific, substantial, and credible by a person of ordinary skill in the art in view of all evidence of record. Office personnel are reminded that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement. Similarly, Office personnel must accept an opinion from a qualified expert that is based upon relevant facts whose accuracy is not being questioned; it is improper to disregard the opinion solely because of a disagreement over the significance or meaning of the facts offered. (emphasis added).

Furthermore, in rebutting a *prima facie* showing of lack of utility, an applicant does not have to provide evidence sufficient to establish that an asserted utility is true "beyond a reasonable doubt." *In re Irons*, 340 F.2d 974, 978, 144 U.S.P.Q. 351, 354 (C.C.P.A. 1965). Instead, evidence will be sufficient if, considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true. It is respectfully submitted that the evidence of record, which includes not only the Declaration but also numerous accounts from the pharmaceutical industry, more than fulfills the Applicant's burden of proof.

B. *Recombinant Yeast Cells Comprising Orphan G Protein-Coupled Receptors Are Useful For Ligand Identification*

Applicants further maintain their position that screening assays are one of the categories of inventions that M.P.E.P. §2107.01 specifically lists as having "a clear, specific and *unquestionable* utility (e.g., they are useful in analyzing compounds)." (Emphasis added.) The utility of the claimed yeast cells lies in their ability to screen for and identify ligands that modulate the surrogate yeast signal transduction activity as described herein and in the Declaration. The singular result of identifying such ligands is useful under § 101 for modulation of the signal transduction activity.

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In response to the Applicants' position, it is stated that "research tools are useful only where they can be used in conjunction with other method steps to evaluate materials other than themselves or to arrive at some result." (Office Action dated June 14, 2005, page 4, first paragraph.) This is precisely the object of the claimed yeast cells—to evaluate other materials (e.g., ligands) and their effect on the biological function provided by the G protein-coupled receptors (e.g., signal transduction and adenylyl cyclase, phospholipase C modulation).

Contrary to the assertion in the Office Action, the claimed yeast cells are not used to evaluate themselves. The claimed yeast cells are "not the subject of basic research". No further research on the claimed recombinant yeast cells is required to make the yeast cells and to use them in the screening assays disclosed in the application. If a putative ligand is screened and is found to modulate the receptor by generation of a detectable signal, the invention has been achieved and the method is complete. No further research is required to complete conduct of the invention.

Although the information generated by conduct of the invention may be used in further research, that further research is not directed to the claimed recombinant yeast cells themselves. It may be directed to the ligand identified, or the receptor, but neither the ligand nor the receptor is claimed. Moreover, this is the heart of a research tool and research tools are patentable. See M.P.E.P. §2107.1

Moreover, the research tool embodied by the instant invention is no different than numerous other research tools for which patents have been granted. For example, there have been numerous patents granted on mass spectrometers. Mass spectrometers are well known research tools widely used to identify unknown compounds, many of which have no known utility. The data output of a mass spectrometer provides a mass profile of complex mixtures of compounds. Although further research, using the data output from the mass spectrometer, will be required to identify the compounds in the mixture, and further research may even be required to identify and/or confirm the useful properties of one or more compounds in the mixture, the mass spectrometer nevertheless has a specific and substantial asserted utility or a well established utility. The Patent Office has recognized as much in the patents that it has granted covering such research tools.

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The instant rejection appears to be based, at least in part, on the role of the ligand in providing a biological function. (Office Action dated June 14, 2005, page 3, first paragraph.) Applicants reiterate that it is not the ligands that are claimed, but rather, the cells upon which they will act. Therefore, any role that the ligands play "in the modulation or identification of any disease state" is irrelevant. Furthermore, there is no legal or administrative authority that requires, as the Examiner suggests, that a biological activity must be associated with the modulation or identification of "a disease state" in order to satisfy the utility requirements under §§ 101 and 112. It is more than enough to know that the identified ligands will modulate a well-known intracellular signal transduction pathway to produce a biological response.

B. Reliance on *Brenner v. Manson* is Misplaced

The lack of utility rejection, as reiterated in the instant Office Action, is premised on the case of *Brenner v. Manson*, 383 U.S. 519, 148 U.S.P.Q. 689 (S. Ct. 1966), which was cited on page 4 of the Office Action dated April 19, 2004. Specifically, the Office Action suggested that the Supreme Court in *Brenner* held that "a research utility was not considered a 'substantial utility'." (April 19, 2004 Office Action, p. 4, second para. last sent.). The Supreme Court in *Brenner* made no such holding or suggestion.

In *Brenner*, the claims at issue were directed to a novel process for making known steroid compounds whose utility--other than as a possible object of scientific inquiry-- had not yet been evidenced. The Supreme Court held that in this situation, the claimed process lacked a specific utility because the compounds produced by the process were not shown to have a specific utility.

However, contrary to the assertion in the April 19, 2004 Office Action, the *Brenner* court clearly did not hold that "a research utility was not considered a 'substantial utility'." Indeed, a research utility is at the heart of research tools, such as mass spectrometers, which the Patent Office has recognized constitutes sufficient utility under 35 U.S.C. §101. Moreover, as noted above, M.P.E.P. §2107.1 specifically lists the type of research tool at issue in the instant application, i.e., screening assays, as having a clear,

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specific and *unquestionable* utility (e.g., they are useful in analyzing compounds)." (Emphasis added.)

Furthermore, unlike the fact pattern presented in *Brenner, supra*, the instant application is not claiming a process for making orphan G protein-coupled receptors, or for making compounds that are putative ligands of orphan G-proteins receptors. Rather, the present application claims recombinant yeast cells that are used in screening assays to identify compounds, e.g., ligands that modulate orphan G protein-coupled receptors.

Therefore, the claimed yeast cells have utility as research tools. As noted above, the utility of such research tools has been recognized by the Patent Office. Moreover, the well-established, real world utility of such research tools is evidenced by documentation provided by Applicants in their response dated October 19, 2004, which shows real world companies have paid large amounts of real world money to obtain the rights to use similar cells for the purpose of screening compounds to identify ligands of orphan G protein-coupled receptors. Accordingly, the facts of *Brenner v. Manson* are inapposite to the facts of the instant application and reliance by the Examiner on *Brenner v. Manson* as the basis for a finding of lack of utility is misplaced.

Therefore, in accord with the M.P.E.P. and applicable case law, an asserted utility has been provided for the claimed invention that is specific, substantial, and credible, and would be considered as much by a person of ordinary skill in the art in view of all evidence of record. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

Claims 1, 2, 5, 8-11, 17, 25-27, 36, 37, 39, 50, 51, 53, 77 and 78 are rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement. Applicants respectfully traverse the rejection for the reasons of record and reiterate those reasons herein.

The Examiner appears to maintain the allegation that because the invention as claimed does not have utility, a person skilled in the art would not be able to use the invention as claimed without undue experimentation, and as such, the claim is defective under 35 U.S.C. § 112, first paragraph. In this regard, M.P.E.P. § 2164.07 provides that a

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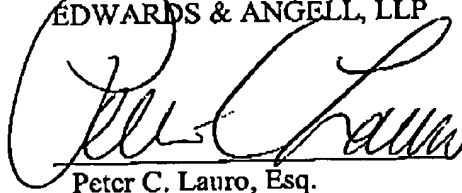
35 U.S.C. § 112, first paragraph, rejection should not be imposed or maintained unless an appropriate basis exists for imposing a rejection under 35 U.S.C. § 101. For the reasons of record set forth in the responses filed on January 2, 2004, October 19, 2004 and April 11, 2005 and for the further reasons discussed in detail above it is respectfully submitted that the rejection under 35 U.S.C. § 101 is improper and should be withdrawn.

M.P.E.P. § 2164.07 further provides that any rejection under 35 U.S.C. § 112, first paragraph, based on grounds other than "lack of utility" should be imposed separately from any rejection imposed due to "lack of utility" under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph. The grounds for rejection given by the Examiner do not appear to include any basis other than the alleged lack of utility. Applicants maintain that such grounds for rejection are improper and therefore, respectfully request reconsideration and withdrawal of the rejection.

CONCLUSION

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of all pending rejections, and allowance of this application with claims 1, 2, 5, 8-11, 17, 25-27, 36, 37, 39, 50, 51, 53, 77 and 78. If a telephone call or personal interview with Applicants' attorney would be helpful in expediting prosecution of the application, the Examiner is invited to call the undersigned at the telephone number indicated below.

Respectfully submitted,
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